REMARKS/ARGUMENTS

In this Amendment After Final Under 37 C.F.R. § 1.116 ("Second AAF"), Applicants propose to amend claims 22, 23, and 36-38 in order to better define the claimed invention and to improve clarity. No new matter is introduced.

Prior to entry of the Second AAF, claims 22-41 were pending in the application. After entry of the Second AAF, claims 22-41 remain pending in the application.

In the Third FOA, the Examiner rejected claims 22-30 and 35-41 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 3,838,752 to Berkovitz ("Berkovitz I")[1] in view of U.S. Patent No. 5,429,211 to Aulanko et al. ("Aulanko I"),[2] U.S. Patent No. 5,975,826 to Scholder ("Scholder"), and U.S. Patent No. 4,158,283 to Nation ("Nation"); and rejected claims 31-34 under 35 U.S.C. § 103(a) as being unpatentable over Berkovitz I in view of Aulanko I, Scholder, and Nation, and further in view of World Intellectual Property Organization International Publication No. WO 99/43595 to Hollowell et al. ("Hollowell").

Entry of Second AAF

Applicants submit that the amendments to claims 22, 23, and 36-38 in this Second AAF do not raise new issues that would require further consideration and/or search, and do not raise the issue of new matter.

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[1] Labeled as Berkovitz I in order to distinguish it from previously cited U.S. Patent No. 4,030,569 to Berkovitz ("Berkovitz II").

[2] Labeled as Aulanko I in order to distinguish it from previously cited U.S. Patent No. 5,665,944 to Aulanko et al. ("Aulanko II").

Additionally, Applicants submit that the amendments to claims 22, 23, and 36-38 in this Second AAF place the application in better form for appeal by materially reducing or simplifying the issues for appeal. Therefore, Applicants submit that this Second AAF should be entered and considered by the Examiner.

Incorporation of Previous Arguments by Reference

In addition to the arguments presented below, Applicants specifically incorporate by reference the arguments made in the Amendment Under 37 C.F.R. § 1.111 ("First Amend") filed on January 3, 2006; the Amendment After Final Under 37 C.F.R. § 1.116 ("First AAF") filed on November 1, 2006; the Amendment Under 37 C.F.R. § 1.111 ("Second Amend") filed on July 16, 2007; the Amendment Under 37 C.F.R. § 1.111 ("Third Amend") filed on April 22, 2008; the Amendment Under 37 C.F.R. § 1.111 ("Fourth Amend") filed on November 28, 2008; the Amendment Under 37 C.F.R. § 1.114 ("First 114 Amend") filed on July 24, 2009; and the Amendment Under 37 C.F.R. § 1.111 ("Fifth Amend") filed on November 23, 2009.

In re Aller

As discussed in the First 114 Amend, the Third FOA's statement that "it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art" (Third FOA, p. 5, § 30; p. 6, § 32; p. 6, § 34; and p. 7, § 39)

demonstrates a misplaced reliance on In re Aller, 105 USPQ 233 (CCPA 1955) (copy submitted with the First 114 Amend).

In In re Aller, a single prior art reference disclosed an identical chemical process, with the exception of the temperature and sulfuric acid concentration involved. The alleged invention involved lowering the temperature and raising the sulfuric acid concentration. In stark contrast, the Third FOA is attempting to combine portions of four references:

> a first reference (Berkovitz I) from primary U.S. Classification 187/20 (and secondary U.S. Classifications 187/27 and 184/15);
>
> a second reference (Aulanko I) from primary U.S. Classification 187/254 (and secondary U.S. Classification 187/406);
>
> a third reference (Scholder) from primary U.S. Classification 414/444 (and secondary U.S. Classifications 414/490 and 254/4); and
>
> a fourth reference (Nation) from primary U.S. Classification 57/200 (and secondary U.S. Classifications 75/175.5 and 148/11.5).

The Third FOA's attempt to rely on Scholder to disclose "wherein each cable of the plurality of [parallel] carrier cables has a nominal diameter greater than 5 mm and less than 7 mm" (independent claims 22, 36, and 37) appears to indicate that the Examiner was unable to find any reference in at least U.S. Classification 187/XXX or 184/XXX that discloses, teaches, or suggests this recitation. The Third FOA does not appear to contradict this argument.

Similarly, the Third FOA's attempt to rely on Nation to disclose "wherein a ratio of a diameter of the drive sheave to a nominal diameter of each cable of

the plurality of [parallel] carrier cables is greater than or equal to 30:1 and less than or equal to 40:1" (independent claims 22 and 37) and "wherein a ratio of a diameter of the drive sheave to a nominal diameter of each cable of the plurality of [parallel] carrier cables is substantially 30:1" (independent claim 36) appears to indicate that the Examiner was unable to find any reference in at least U.S. Classification 187/XXX or 184/XXX that discloses, teaches, or suggests either of these recitations. The Third FOA also does not appear to contradict this argument.

Thus, Applicants submit that In re Aller is not logically relevant to the Examiner's argument at least because this is not a situation in which the general conditions of the claim are disclosed in the prior art. As a result, the Third FOA's reliance on In re Aller is misplaced.

In re Rice

As discussed in the Fifth Amend, the Third FOA's statement that "[m]inor differences between the prior art and a claimed device may be a matter of design choice absent evidence to the contrary" (Third FOA, p. 5, § 30; p. 6, § 32; p. 6, § 34; and pp. 7-8, § 39) demonstrates a misplaced reliance on In re Rice, 144 USPQ 476 (CCPA 1965) (copy submitted with the Fifth Amend), a case not cited in the MPEP.

In addition, Applicants submit that, as discussed below, the differences between the prior art and the recitation "wherein each cable of the plurality of

[parallel] carrier cables has a nominal diameter greater than 5 mm and less than 7 mm" are not minor and, thus, are not a simple matter of design choice.

Thus, Applicants submit that In re Rice is not logically relevant to the Examiner's argument at least because this is not a situation in which the differences between the prior art and the claimed device are minor. As a result, the Third FOA's reliance on In re Rice is misplaced.

In re Woodruff

As discussed in the Fifth Amend, the Third FOA's statement that "[w]here the difference between the claimed invention and the prior art is some range or other variable within the claims the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range" (Third FOA, p. 5, § 30; p. 6, § 32; pp. 6-7, § 34; and p. 8, § 39) demonstrates a misplaced reliance on In re Woodruff, 16 USPQ2d 1934 (Fed. Cir. 1990) (copy submitted with the Fifth Amend).

Applicants submit that the Safety Code for Elevators and Escalators A17.1 (issued by the American Society of Mechanical Engineers), paragraph 2.20.4, requires a minimum diameter of 9.5 mm for hoisting and counterweight ropes. Applicants also submit that a person having ordinary skill in the art ("PHOSITA") generally is not motivated to intentionally violate safety codes set up by standard-setting organizations in their field. Thus, Applicants' ability to make a safe and reliable elevator in which each cable of

the plurality of [parallel] carrier cables has a nominal diameter greater than 5 mm and less than 7 mm demonstrates both utility and nonobviousness, in that it achieves unexpected results. For at least these reasons, Applicants submit that the Third FOA's reliance on In re Woodruff is misplaced.

In re Keller and In re Merck

Applicants submit—at least to the extent that Applicants' arguments point out specific misinterpretations of individual references of the cited art in the Third FOA (or other Office Actions)—Applicants are not "attacking references individually" (see In re Keller, 208 USPQ 871 (CCPA 1981) and In re Merck, 231 USPQ 375 (Fed. Cir. 1986)). In other words, Applicants' arguments are not attempting to read the individual references in isolation as opposed to what the references fairly teach in combination with the prior art as a whole, but attempting to correct and/or clarify specific misinterpretations of the individual references used as a basis for determining what the references fairly teach in combination with the prior art as a whole.

Section 103(a) Rejection—Berkovitz I/Aulanko I/Scholder/Nation

Applicants submit that independent claims 22, 36, and 37, as amended, are patentable under 35 U.S.C. § 103(a) over any proper combination of Aulanko I, Berkovitz I, Nation, and/or Scholder for at least the following reasons.

First, Applicants concur with the Third FOA's admissions that Berkovitz I does not disclose at least "an elevator without machine room", "cage guide

rails", "counterweight guide rails", "wherein the cage is guided by the cage guide rails", "wherein the counterweight is guided by the counterweight guide rails", "wherein each cable of the plurality of [parallel] carrier cables has a nominal diameter greater than 5 mm and less than 7 mm", "wherein the undercut portions have a width greater than 1 mm and less than 3 mm", and "wherein a ratio of a diameter of the drive sheave to a nominal diameter of each cable of the plurality of [parallel] carrier cables is greater than or equal to 30:1 and less than or equal to 40:1". Third FOA, pp. 3-4, § 18.

Second, the Third FOA's purported argument appears to gloss over significant differences between the prior art in Berkovitz I and the invention of Berkovitz I. Applicants submit that FIGs. 3A, 6A, 6B, and 9A refer to the prior art of Berkovitz I, while FIGs. 3B, 7A, 7B, and 9B refer to the invention of Berkovitz I. Thus, the Third FOA's reference to drive sheave 82, secondary sheave 84, rope 86, and double-wrap roping in FIG. 6A (id., p. 3, § 12) relates to the prior art in Berkovitz I. Similarly, the Third FOA's reference to undercut portions 32 in FIG. 3A (id., p. 3, § 15) relates to the prior art in Berkovitz I. And the corresponding ratio W/D = 0.75 (Berkovitz I, c. 3/ll. 54-62) relates to the prior art in Berkovitz I. In contrast, the ratio W/D = 0.375 (id., c. 5/ll. 54-62) cited in the Third FOA (Third FOA, p. 3, § 16) relates to the invention of Berkovitz I in which double-wrap roping is not used.

Third, Applicants submit that Scholder is not analogous art to the present application. Scholder is entitled "Hand-Truck With Attachments". In

contrast, Berkovitz I is entitled "Elevator System", Aulanko I is entitled "Traction Sheave Elevator", and Nation is entitled "Cable Stress and Fatigue Control". Also, as shown on their cover pages, Berkovitz I is primary U.S. Classification 187/20 (and secondary U.S. Classifications 187/27 and 184/15), Aulanko I is primary U.S. Classification 187/254 (and secondary U.S. Classification 187/406), and Nation is primary U.S. Classification 57/200 (and secondary U.S. Classifications 75/175.5 and 148/11.5). Applicants submit that this demonstrates not only that Scholder is not analogous art, but that the Examiner was unable to find any reference in at least U.S. Classification 57/XXX, 184/XXX, or 187/XXX that even arguably disclosed "wherein each cable of the plurality of [parallel] carrier cables has a nominal diameter greater than 5 mm and less than 7 mm".

Applicants also submit that there is no common primary or secondary U.S. Patent Classification System ("USPC") Classification between Scholder and any of Aulanko I, Berkovitz I, and Nation.

Additionally, Applicants submit that there is no common Field of Search between Scholder and any of Aulanko I, Berkovitz I, and Nation.

Fourth, Applicants submit that Scholder is not reasonably pertinent to the particular problem with which the present invention is concerned. For example, the cables of Scholder—which are not a plurality of parallel carrier cables—have the dimensions listed because they are suitable for hand-trucks (e.g., the title of Scholder is "Hand-Truck With Attachments". As a result,

Applicants submit that a PHOSITA would not attempt to combine Scholder with Aulanko I, Berkovitz I, and/or Nation, as the Examiner has attempted to do.

Fifth, Applicants submit that Scholder effectively teaches away from use in elevator applications (as opposed to hand-truck applications). The recitation "wherein each cable of the plurality of [parallel] carrier cables has a nominal diameter greater than 5 mm and less than 7 mm" is contrary to what a PHOSITA typically would use. That is, ropes used in an elevator generally require a minimum wire thickness. For example, the Safety Code for Elevator and Escalators A17.1 paragraph 2.20.4 (issued by the American Society of Mechanical Engineers) requires a minimum diameter of 9.5 mm for hoisting and counterweight ropes. In contrast, the cables disclosed in Scholder are approximately 5 mm in diameter (Scholder, c. 5/ll. 56-57). For this reason, as well, Applicants submit that a PHOSITA would not attempt to combine Scholder with Aulanko I, Berkovitz I, and/or Nation, as the Examiner has attempted to do.

Sixth, amended independent claims 22, 36, and 37 recite, inter alia, "wherein the cage is configured to accommodate human passengers" (emphasis added). Applicants submit that a PHOSITA would not look to Scholder for disclosures, teachings, or suggestions related to elevators whose cage is configured to accommodate human passengers. For this reason, too, Applicants submit that a PHOSITA would not attempt to combine Scholder

with Aulanko I, Berkovitz I, and/or Nation, as the Examiner has attempted to do.

Seventh, Nation effectively teaches away from steel cables in favor of titanium cables and/or aluminum cables. Nation, Abstract and Background of the Invention. For example, Applicants submit that cited language in the Third FOA (e.g., p. 4, § 27) is referring to advantages of titanium cables. As a result, Applicants submit that a PHOSITA would not attempt to combine Nation with Aulanko I, Berkovitz I, and/or Scholder, in order to arrive at a plurality of parallel carrier cables in which each cable is a steel cable, as the Examiner has attempted to do.

For all of these reasons, Applicants submit that amended independent claims 22, 36, and 37 are patentable under 35 U.S.C. § 103(a) over any proper combination of Aulanko I, Berkovitz I, Nation, and/or Scholder. Applicants further submit that dependent claims 23-30, 35, and 38-41 are patentable under 35 U.S.C. § 103(a) over any proper combination of Aulanko I, Berkovitz I, Nation, and/or Scholder, for at least the same reasons as amended independent claims 22 and 37, from which claims 23-30, 35, and 38-41 directly or indirectly depend.

Section 103(a) Rejection—Berkovitz I/Aulanko I/Scholder/Nation/Hollowell

Applicants submit the Third FOA does not argue that Hollowell overcomes the deficiencies of Aulanko I, Berkovitz I, Nation, and Scholder discussed above. Therefore, Applicants submit that dependent claims 31-34

are patentable under 35 U.S.C. § 103(a) over any proper combination of Aulanko I, Berkovitz I, Hollowell, Nation, and/or Scholder, for at least the same reasons as amended independent claim 22, from which claims 31-34 directly or indirectly depend.

Request for Reconsideration and Allowance

Accordingly, in view of the above amendments and remarks, reconsideration of the rejections and allowance of each of claims 22-41 in connection with the present application is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

If necessary, the Director of the U.S. Patent and Trademark Office is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; in particular, extension of time fees.

Respectfully submitted,

HARNESS, DICKEY & PIERCE, P.L.C.

By _____

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JAC/LFG:vrj

We do not find it necessary to reach the other rejections.

Affirmed.

Court of Customs and Patent Appeals

In re Keller, Terry, and Davies

No. 80-573
Decided Feb. 12, 1981

PATENTS

1. Words and phrases (§70)

Term "cardiac pacer" encompasses both implantable and non-implantable devices.

2. Patentability — New use or function — Analogous art (§51.5573)

Stimulator used in studies of atrioventricular conduction system of mammalian heart is not so nonanalogous to stimulator used to pace mammalian heart that references disclosing each may not be combined.

3. Patentability — Anticipation — Combining references (§51.205)

Pleading and practice in Patent Office — Rejections (§54.7)

It is not necessary that device shown in one reference can be physically inserted into device shown in other reference to justify combining their teachings in support of rejection.

4. Patentability — Anticipation — Combining references (§51.205)

Patentability — Invention — In general (§51.501)

Test of obviousness is not whether features of secondary reference may be bodily incorporated into primary reference's structure, nor whether claimed invention is expressly suggested in any one or all of references; rather, test is what combined teachings of references would have suggested to those of ordinary skill in art.

5. Court of Customs and Patent Appeals — Issues determined — Ex parte patent cases (§28.203)

Patentability — Invention — In general (§51.501)

Pleading and practice in courts — Burden of proof — In general (§53.131)

Pleading and practice in Patent Office — In general (§54.1)

Burden shifts to applicant, once prima facie case of obviousness is established, to rebut such case with objective evidence of nonobviousness; both Court of Customs and Patent Appeals and Patent Office must give full consideration to evidence introduced to so rebut, and render decision based on relative strength of applicant's showing and prima facie case established by references; such showing may shift burden of proof to examiner to then come forward with further support for his conclusion that invention would be obvious under conditions stated in Section 103; however, whether showing does shift burden of proof must be determined on case by case basis.

6. Patentability — Anticipation — Combining references (§51.205)

Patentability — Invention — In general (§51.501)

One cannot show nonobviousness by attacking references individually where rejections are based on combinations of references.

7. Evidence — Expert testimony (§36.10)

Evidence — Weight and credibility (§36.40)

Patentability — Anticipation — Combining references (§51.205)

Patentability — Invention — In general (§51.501)

Opinion of affiant on ultimate legal question of obviousness is entitled to little weight in appeal in which test is not whether suggestion to use certain item in particular device is found in single prior art reference, which was test applied by affiant, but rather what two combinations of three references would have suggested to one of ordinary skill in art.

8. Oath (§47)

Pleading and practice in Patent Office — Rules effect (§54.9)

Reissue — In general (§58.1)

Reissue oath or declaration filed under Patent Rule 175(a)(4) must also comply with both subsections (a)(5) and (a)(6); subsection (a) of Patent Rule 175 sets forth requirements relating to content of statement that must be filed by applicant with his reissue application; subsection (a)(4), which requires applicant to particularly specify prior art or other information rele-

vant to patentability not previously considered by Patent Office that might cause examiner to deem original patent wholly or partly inoperative or invalid, thus requires prior art or other information to be specified in that statement.

9. Oath (§47)

Pleading and practice in Patent Office — Rules effect (§54.9)

Reissue — In general (§58.1)

Patent Rule 175(a) requires statement specifying prior art or other information to be made by applicant under oath or declaration; this statement must be subscribed to by applicant, and must either be sworn to or affirmed by applicant as provided in Patent Rule 66 or include personal declaration of applicant as prescribed in Patent Rule 68.

10. Oath (§47)

Pleading and practice in Patent Office — Rules effect (§54.9)

Reissue — In general (§58.1)

Reissue declaration that purports to incorporate by reference paper entitled "citation to prior art," on which prior art being brought to attention of Patent Office by applicant was delineated, that was not subscribed by applicant and did not include applicant's personal declaration, but was subscribed by applicant's attorney, does not comply with Patent Rule 175(a)(4) where, although citation of prior art is dated one day earlier than declaration, there is no evidence that applicant even saw citation at time declaration was executed

Particular patents — Cardiac Pacer

Keller, Terry, and Davies, Digital Counter Driven Pacer, rejections of claims 1, 2, 6, 7, 9-11, 13, and 14 based on prior art affirmed; rejections of claims 1, 2, 6, 7, and 9-16 based on Patent Rule 175(a)(4) affirmed and on 175(a) (5) and (a)(6) reversed.

Appeal from Patent and Trademark Office Board of Appeals.

Application for reissue of patent of John W. Keller, Jr., Reese S. Terry, Jr., and Gomer L. Davies, Serial No. 865,610, filed Dec. 29, 1977, to reissue Patent No. 3,557,796, issued Jan. 26, 1971, on application, Serial No. 805,714, filed Mar. 10, 1969. From decision rejecting all claims, applicants appeal. Modified.

Henry D. Pahl, Jr., Boston, Mass., and Gilbert H. Hennessey, Washington, D.C., for appellants.

Joseph F. Nakamura (Thomas E. Lynch, of counsel) for Patent and Trademark Office.

Before Markey, Chief Judge, and Rich, Baldwin, Miller, and Nies, Associate Judges.

Nies, Judge.

This appeal is from the decision of the Patent and Trademark Office (PTO) Board of Appeals (board) in reissue application serial No. 865,610, filed December 29, 1977,[1] for "Digital Counter Driven Pacer." Claims 1, 2, 6, 7, and 9-16 (all of the claims in the application) stand rejected on the ground of a defective reissue declaration, and claims 1, 2, 6, 7, 9-11, 13, and 14 are rejected on the ground of obviousness in view of the following references:

Inventor	*U.S. Patent No.*	*Issue Date*
Keller, Jr. (Keller)	3,253,596	May 31, 1966
Berkovits	3,345,990	Oct. 10, 1967

Walsh and Moore (Walsh), *The American Journal of Medical Electronics*, First Quarter, 1966, pages 29-34.

Claim 12 is allowable over the art of record but is objected to on the ground that the claim depends from a rejected claim. Claims 15 and 16 are allowable over the art of

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[1] The application requests reissuance of U.S. Patent No. 3,557,796 issued January 26, 1971, on application serial No. 805,714, filed March 10, 1969, by Cordis Corporation, the assignee. Protests were filed against the reissue application by Cardiac Pacemakers, Inc. (CPI) and by Norman H. Stepno of the firm of Bacon & Thomas pursuant to the provisions of 37 CFR 1.291. A brief amicus curiae for protestor CPI was filed in this appeal. Two cases have been filed in the United States District Courts involving appellant's '796 patent:

(1) Cordis Corp. v. Cardiac Pacemakers, Inc. and Edward J. Luczek, United States District Court, District of Massachusetts, Civil Action No. 77-3044-F (infringement action); and

(2) Cardiac Pacemakers, Inc. v. Cordis Corp., United States District Court, District of Minnesota, Fourth Division, Civil Action No. 4-77-427 (declaratory judgment action).

record.[2] We affirm in part and reverse in part.

Claims 1, 2, 6, 7, and 9-16[3] are rejected under 35 USC 251 on the ground that the declaration made by applicant to support the reissue application does not particularly specify the prior art being brought to the attention of the examiner as required by 37 CFR 1.175(a)(4), does not particularly specify the errors relied upon by applicant and how the errors arose as required by 37 CFR 1.175(a)(5), and does not state that the errors arose "without any deceptive intention" on the part of applicant as required by 37 CFR 1.175(a)(6).[4]

Claims 1, 2, 6, 7, 9, 10, 11, 13, and 14 are rejected as unpatentable in view of Keller taken with Walsh. Claims 1 and 2 are further rejected as unpatentable in view of Berkovits taken with Walsh. The statutory basis of these rejections is 35 USC 103.

The Invention

The claimed invention is a cardiac pacer having a digital counter.

As background, the specification explains:

> In the normal heart, electrical signals are generated and appear in the atrium at a rate of approximately 60 to 120 times per minute, depending on such factors as body size and amount of physical exertion. Approximately 0.1 second after such a signal has appeared in the atrium, it is transferred to the ventricle of the heart, which reacts to the stimulation by contracting. This contraction forces blood from the ventricle into the arterial system and thence to the entire body. The delay between the appearance of an electrical signal in the atrium and its appearance in the ventricle is called the A-V delay. Following the contraction of the ventricle, there is an insensitive period lasting about 0.4 second, during which time the heart is unresponsive to electrical pulses. This time is referred to as the refractory delay period.
>
> A common type of heart failure is irregularity in the generation of atrial potentials. In some cases, these potentials appear at only a low rate; in others, they cease entirely for extended periods though at other times the signals may be generated with perfect regularity. It is in persons suffering from this kind of cardiac disorder that a standby or so-called demand mode pacer is used. This device is designed to apply stimulating pulses to the ventricle, by means of an electrode implanted therein, only when the heart fails to generate pulses spontaneously. When natural pulses regularly appear, the pacer provides no stimulation; when they appear irregularly, the pacer adjusts its timing to integrate its artificial pulses with the natural ones. This type of pacer is often provided with circuitry which simulates the refractory delay period of the heart. The reason for including such delay circuitry is that a spontaneous electrical signal which appears a short time after delivery of an artificial pulse is ineffective to pump blood, either because the natural refractory period of the heart caused the heart to ignore the spon-

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[2] In addition to Keller, Berkovits, and Walsh, numerous other references were before the examiner. The examiner indicated in an Office Action dated May 8, 1978, however, that these other references were not any more pertinent than Keller, Berkovits, and Walsh.

[3] Claims 1-12 were included in the reissue application as filed. By preliminary amendment claim 1 was amended and new claims 13 and 14 added. By subsequent amendment claims 3, 4, 5, and 8 were cancelled and new claims 15 and 16 added, the latter two claims reciting in independent form the same subject matter of cancelled dependent claims 5 and 8, respectively. Claims 9-12 were not amended during prosecution of the reissue application.

[4] 37 CFR 1.175 (1980) reads, in pertinent part:

§1.175 Reissue oath or declaration.

(a) Applicants for reissue, in addition to complying with the requirements of the first sentence of §1.65, must also file with their applications a statement under oath or declaration as follows:

* * *

(4) When the applicant is aware of prior art or other information relevant to patentability, not previously considered by the Office, which might cause the examiner to deem the original patent wholly or partly inoperative or invalid, particularly specifying such prior art or other information and requesting that if the examiner so deems, the applicant be permitted to amend the patent and be granted a reissue patent.

(5) Particularly specifying the errors or what might be deemed to be errors relied upon, and how they arose or occurred.

(6) Stating that said errors, if any, arose "without any deceptive intention" on the part of the applicant.

* * *

[24 FR 10332, Dec. 22, 1959, as amended at 29 FR 18503, Dec. 29, 1964; 34 FR 18857, Nov. 26, 1969; 42 FR 5594, Jan. 28, 1977]

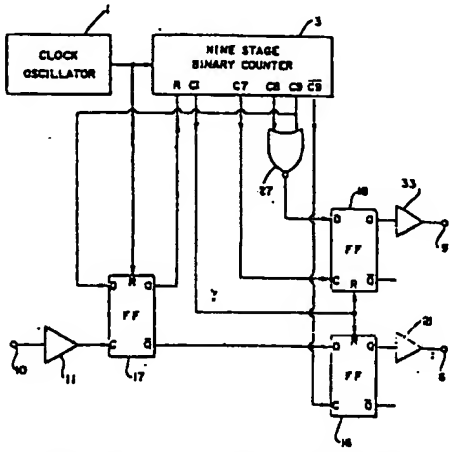
taneous pulse or because the ventricle has not had time following the previous beat to be refilled with blood. A simulated refractory period causes the pacer likewise to ignore these ineffective beats. The device's timing continues just as if the beats had never occurred.

Another form of heart disease is the so-called A-V block in which the patient's heart undergoes normal or near-normal atrial contraction but the atrial signal is not transferred to the ventricle. With such a patient, it is desirable to use a so-called synchronous pacer which detects atrial signals and supplies to the ventricle a stimulating pulse about 0.1 second later, a period which constitutes a simulated A-V delay. In the absence of detected atrial signals, the pacer supplies ventricular pulses at a fixed rate. The synchronous pacer, like the demand pacer, is often provided with refractory delay simulation.

Summarizing the invention, the specification states:

> [A] cardiac pacer according to the present invention times various events and delays by means of a digital counter which is driven by an oscillator operating at a frequency which is a relatively large multiple of a normal heartbeat rate. A cardiac stimulating pulse is generated at a predetermined point in the count. Thus, if the counter cycles repetitively, the heart is stimulated at a predetermined fixed rate. To provide demand mode operation, the counter is reset in response to spontaneous cardiac signals thereby to prevent stimulation when the heart is functioning normally. To provide synchronous mode operation, the counter is reset to a point preceding the stimulation count by an amount which simulates a normal A-V delay.
>
> The use of digital count down circuitry permits both the various delays and the durations of the stimulating pulses to be accurately timed. Further, by counting down from a relatively high frequency, an oscillator having a relatively short duty cycle may be used so as to reduce battery drain. Further, the use of a relatively short oscillator period permits timing components, e.g., capacitors, of relatively small size to be used.

A block diagram of a cardiac pacer, according to the present invention, appears below:



[FF indicates D-TYPE FLIP-FLOP]

The specification indicates that if the pacer is to operate in the demand mode in a particular patient, an output electrode implanted in the patient's heart at a location suitable for stimulating ventricular contractions is connected to output terminal 6 of the pacer. If the pacer is to operate in the synchronous mode in a particular patient, an output electrode implanted in the patient's heart at a location suitable for stimulating ventricular contractions is connected to output terminal 9 of the pacer.

According to the specification, for demand mode operation an input electrode implanted to detect ventricular signals of the patient's heart is connected to input terminal 10 of the pacer. For synchronous mode operation, an input electrode implanted to detect atrium signals of the patient's heart is connected to the input terminal 10. "Cardiac signals applied to the input terminal 10 are amplified and shaped by means of an amplifier 11 so as to be squared into waveforms suitable for use with digital circuitry, as is understood by those skilled in the art."

The timing of the different events occurring in the operation of appellant's pacer is provided by a digital counter 3.

> The counter is driven by an oscillator 1 which establishes the time base. As illustrated, counter 3 comprises a nine stage binary divider and the oscillator 1 runs at a frequency which is relatively high with respect to the contemplated range of heartbeat rates or frequencies. * * *
>
> As is conventional, counter 3 provides a two-stage output signal for each stage of binary division * * *

As is also conventional, the counter 3 runs cyclically, that is, the states of the binary output signals pass through a sequence which repeats after all the possible combinations have been utilized. * * * Further, the counter may at will be reset to a predetermined starting point by the application of a reset signal to a reset terminal, designated R. The starting point of the counter is considered herein to be the zero count and the various possible states or counts are considered to be zero through 511.[5]

In describing operation of the pacer in the demand mode, the specification states that:

> * * * if the patient's heart is beating normally at a rate which is more than the free running rate of the pacer, i.e. about 70 beats per minute, and not more than twice that rate, i.e. about 140 beats per minute, the counter 3 will be reset to its zero count by each natural heartbeat before a count of 511 is reached. Thus, the patient's heart will not be stimulated at all if it is beating spontaneously within this 2-to-1 range of rates. However, if no spontaneous heartbeat is detected between count 256 and count 511, the pacer will then stimulate the patient's heart at the end of the full count period, that is, after a period which corresponds to the 70 pulse per second free running rate. In other words, the difference between the starting point count and the end of the counting sequence establishes a maximum interval between heartbeats. Accordingly, if the spontaneous heart signals disappear intermittently, the pacer will integrate its operation with the normal heartbeat.

In describing operation of the pacer in the synchronous mode, the specification states:

> The resetting of counter 3 is controlled in response to detected signals as described previously. Thus, the counter is reset to its zero count if an atrial signal is detected from count 256 through count 511. A stimulating pulse is then generated at output terminal 9 when count 64 is reached. The delay provided by the interval between the resetting and the 64 count is about 108 milliseconds which satisfactorily simulates the normal A-V delay. Thus the heart is stimulated with timing appropriate for synchronous pacer operation.
>
> * * *
>
> If no atrial signals at all are detected, the counter 3 will run cyclically as described previously and stimulating pulses will be generated at a fixed rate, one pulse being generated each time the counter 3 passes the 64 count.

The specification describes the digital timing circuit in more detail than set forth above. The claims rejected on prior art, however, do not recite such detail. Claims 1 and 13 are illustrative:

> 1. Cardiac pacer apparatus comprising:
> an oscillator providing a pulsating signal at a preselected frequency, which preselected frequency is a relatively large multiple of a normal heart beat rate;
> a cyclically operating digital counter means for counting the pulsations of said pulsating signal;
> means controlled by said counter for generating a cardiac stimulating potential when said counter reaches a predetermined count;
> means for detecting a naturally occurring heart beat; and
> means for setting said counter to a preselected value when a naturally occurring heart beat is detected. [Paragraphing added.]
>
> 13. Cardiac pacer apparatus comprising:
> an oscillator providing a pulsating signal at a preselected frequency, which preselected frequency is a relatively large multiple of a normal heart beat rate;
> a cyclically operating digital counter means for counting the pulsations of said pulsating signal;
> means controlled by said counter for generating a cardiac stimulating potential when said counter reaches a predetermined count;
> means for detecting cardiac signals generated during a heart beat; and
> means responsive to such detected cardiac signals for setting said counter to a starting point count which precedes said predetermined count by a number corresponding to a preselected maximum interval between successive heartbeats whereby a stimulating potential is generated only if said preselected maximum interval elapses between heart beats. [Paragraphing added.]

The References

The Keller '596 Patent

Keller relates to a transistorized, implantable cardiac pacer for regulating an animal

[5] Consequently, the counter counts as follows: 0, 1, 2, 3, * * *, 509, 510, 511, 0, 1, 2, * * *, that is, the count changes from "511" to "0".

heart. The specification states that a pacer according to the Keller invention includes:

> * * * sensing means responsive to a physiological heart pacing signal for producing a trigger signal, means for delaying said trigger signal for a period substantially equal to a normal atrial-ventricular delay,[6] a two-state free running oscillator one state of which can be terminated by the arrival of a delayed trigger signal and the other state of which is unaffected by the arrival of a signal, means responsive to the return of said oscillator to said one state for producing ventricular stimulation, whereby the minimum rate at which the pacer operates is determined by the natural period of the oscillator and the maximum rate at which said pacer can operate is determined by the natural duration of said other state, the natural durations of each of said states being independently predeterminable, and the arrival of delayed trigger signals at frequencies between said minimum and maximum synchronously controls said oscillator.

Identifying the elements described in the Keller patent, the examiner found the Keller pacer includes:

> a pulse generator (comprising blocking oscillator 40, stimulating pulse generator 50, and output amplifier 60);
> an analog time base circuit included in the pulse generator for generating a cardiac stimulating potential at a predetermined time (comprising transistors T5, T6);
> means for detecting cardiac signals (comprising amplifying circuit 10,20);
> reset means for setting the analog time base circuit to a starting point (comprising diode D2); and
> means for inhibiting the resetting during a preselected refractory delay period which ends at a time after the starting time but before the stimulus generating time (comprising delay circuit 30).

Appellant has not disputed these findings.

The Keller pacer can operate in a synchronous mode and in an asynchronous free-running mode. In the synchronous mode, an atrial signal is sensed, amplified, and processed, and a ventricular stimulation pulse produced and applied to the heart a predetermined time after the occurrence of the atrial signal. This predetermined time corresponds approximately to the normal A-V delay. If atrial signals are sensed to occur at a dangerously high rate, the pacer operates in the synchronous mode to produce and apply ventricular stimulation pulses at a predetermined maximum rate. If atrial signals are not sensed or are too weak for synchronization purposes, the pacer operates in the asynchronous free-running mode to produce and apply ventricular stimulation pulses at a predetermined minimum rate.[7]

Both the sensing of the atrial signal and the application of ventricular stimulation are accomplished by electrodes implanted in the patient's heart.

The Berkovits '990 Patent

Berkovits relates to a cardiac pacer for regulating a heart. The specification states that a pacer according to the Berkovits invention includes: means for accurately monitoring the beating action of a human heart; means for providing corrective electrical stimulation of the beating action of an abnormal heart; and means for automatically effecting such corrective heart stimulation only where required as determined by the means for monitoring the heart. The Berkovits pacer functions to "furnish stimulation to an abnormal heart in such a manner that heartbeats are individually stimulated and closely integrated with natural heartbeats."

Identifying the elements described in the Berkovits patent, the examiner found the Berkovits pacer includes:

> an analog time-base pulse generator (comprising heart stimulating means 12 and pulse generating means 18);
> means for detecting a naturally occurring heartbeat (comprising detecting means 14 and amplifying means 16); and
> means for restarting the timing period when a naturally occurring heartbeat is detected (comprising triode clipper 122).

Appellant has not disputed these findings.

The Berkovits pacer is not implantable. The monitoring means 10 includes electrocardiograph means 14 for detecting electrical signals developed by the heart during natural heartbeat action, vacuum tube

[6] According to Keller, the atrial-ventricular (A-V) delay is approximately two-tenths of a second in man, and less in smaller animals.

[7] The minimum rate is 60 pulses per minute for a human patient.

amplifier means 16 for amplifying these natural heart signals, vacuum tube pulse generating means 18 responsive to the amplified signals for sending control signals to vacuum tube heart stimulating means 12, and may also include oscilloscope means 20 and audible signal means 22 for providing visual and audible indications of the occurrence of natural and stimulated heartbeats.

The heart stimulator 12 is equipped with a double-pole triple-throw switch 177 which permits manual selection of the mode of operation of the heart stimulator. Berkovitz states:

> When the movable switch arms 178,180 [of switch 177] are set on the fixed contacts 182,184, respectively, the heart stimulator will not be operative. * * * [W]hen the movable arms are set on the fixed contacts 186,188, the heart stimulator is adapted to provide a continuous series of heart stimulating electrical impulses at a predetermined rate which is independent of natural heartbeats occurring at the same time. * * * [W]hen the movable arms are set on the fixed contacts 190,192 * * * the heart stimulator is adapted to provide heart-stimulating electrical impulses only in closely integrated relation to natural heartbeats * * * so that stimulated and natural heartbeats can each contribute to maintenance of a predetermined heartbeat rate.
>
> * * *
>
> Electrodes 218 of any conventional type * * * can be employed for applying a relatively large heart stimulating pulse to the patient's heart from outside the patient's body whereas the electrodes 220 can be surgically connected to the patient's heart for applying a relatively smaller electrical impulse directly to the patient's heart when desired.

Variable resistor 210 of the heart stimulating means 12 is used to selectively vary the amplitude of the heart stimulating pulse to be applied to the heart through electrodes 218 and 220.

We note that, in addition to the mode selection switch 177 and the stimulating pulse amplitude adjustment control 210 included in the heart stimulating means 12, the amplifier means 16 includes a polarity-reversing switch 32, a bias circuit switch 62, a variable voltage divider 116 which serves as a center control for the oscilloscope means 20, and a variable voltage divider 106,108 which serves as an amplifier gain control. It is apparent from the Berkovits disclosure as a whole that these switches and variable circuit elements are operator controlled.

The Walsh and Moore Article

Walsh relates to a stimulator driving unit for the controlled stimulation of the heart of a mammal. The disclosed driver includes a digital timing circuit. Walsh states:

> A digital timing system was used since it provides a higher degree of accuracy and resetability than the R-C type circuits used in conventional stimulators. In this system, a crystal-controlled, time-base generator provides a standard from which to derive the various intervals. A crystal frequency [of 0.1 megahertz] was chosen to provide a 10-*u* sec time base. The output of this circuit was amplified, shaped and fed to a series of six digital counting modules that make up the timing chain controlling intervals between stimuli.

The examiner found that Walsh discloses:

> * * * the conventional expedient of providing a digital time base means for a medical stimulator by employing an oscillator having a frequency much higher, such [as] a relatively large multiple of the stimulation pulse frequency and counting means to produce a stimulating pulse at the desired frequency.

Appellant has not disputed these findings.

The Rejections

Reissue Declaration Rejections

The examiner rejected claims 1, 2, 6, 7, 13-16 (the claims that were either amended or added during prosecution of the reissue application) under 35 USC 251 as based on an insufficient reissue declaration. The declaration which accompanied the reissue application reads, in pertinent part:

> I, William P. Murphy, Jr., Chairman of the Board of Directors of Cordis Corporation, declare
>
> * * *
>
> [1.] that subsequent to the issuance of U.S. Letters Patent No. 3,557,796, applicant has, in connection with the prosecution of corresponding foreign patent applications, been made aware of prior art relevant to patentability not previously considered by the Patent Office, which

prior art might cause the Examiner to deem the original patent wholly or partly inoperative or invalid;
[2.] that this new prior art is particularly specified in a citation of prior art accompanying this reissue application;

* * *

[3.] that, to the extent the [preliminary] amendment [filed herewith] might be deemed to correct errors in the original patent, such errors arose without any deceptive intent or purpose upon the part of applicant; * * *

* * *

/s/ William P. Murphy, Jr.

* * *

Date: Dec. 24, 1977

The "citation of prior art" referred to in the declaration and filed with the declaration reads, in pertinent part:

The following prior art has become known to applicant subsequent to the issuance of the original Letters Patent No. 3,557,796 and is being brought to the attention of the Patent and Trademark Office for its consideration in connection with this reissue application.
The references are:

* * *

Copies are enclosed.

* * *

/s/ [Attorney for Applicant]

December 23, 1977

In making these rejections, the examiner stated that "applicants [sic] have not particularly specified all the changes in the claims [as set forth in the preliminary amendment] as the errors nor have they stated how they [the errors] arose or occurred."

The board affirmed the examiner and stated that

the declaration fails to particularly specify the newly discovered prior art. Reference to another paper to be filed in the application is inadequate to fulfill this requirement.

The board further indicated that the declaration not only failed to comply with 37 CFR 1.175(a)(4), but also failed to comply with 37 CFR 1.175(a)(5) and (a)(6).[8] Accordingly, pursuant to 37 CFR 1.196(b),[9] the board rejected claims 9-12 (the claims that were neither amended nor added during prosecution of the reissue application) under 35 USC 251 as based on a declaration which does not comply with 37 CFR 1.175(a)(4), (a)(5), and (a)(6).

Prior Art Rejections

The examiner rejected claims 1, 2, 6, 7, 9-11, 13, and 14 as obvious in view of Keller taken with Walsh. He stated:

The claims define over the Keller, Jr. patent in the recitation of a digital time base pulse generator. Walsh et al. discloses in Figure 3 the conventional expedient of providing a digital time base means for a medical stimulator by employing an oscillator having a frequency much higher, such as a relatively large multiple of the stimulation pulse frequency and counting means to produce a stimulating pulse at the desired frequency.

Providing an oscillator and counter-type digital time base generator for its analog equivalent in the Keller, Jr. et al. device amounts to an obvious substitution to one of ordinary skill in the art after consideration of the prior art taken as a whole.

The examiner further rejected claims 1 and 2 as obvious in view of Berkovits taken with Walsh. He stated that it would have been obvious in view of the teachings of Walsh to employ digital timing circuitry with a relatively high frequency oscillator in the Berkovits pacer in place of the analog timing circuitry.

Neither Keller nor Berkovits nor Walsh were cited during prosecution of the original patent application.

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[8] See note 4, supra.
[9] 37 CFR 1.196 (1980) reads, in pertinent part:

§1.196 Decision by the Board of Appeals.

* * *

(b) Should the Board of Appeals have knowledge of any grounds not involved in the appeal for rejecting any appealed claim, it may include in its decision a statement to that effect with its reasons for so holding, which statement shall constitute a rejection of the claims.

* * *

[24 FR 10332, Dec. 22, 1959, as amended at 42 FR 5595, Jan. 28, 1977]

Rebuttal Evidence

To rebut the prima facie case of obviousness established by the examiner, appellant filed an affidavit of Jozef K. Cywinski, Ph.D. This affidavit, according to appellant, "concerns itself mainly with the question of whether the Walsh et al. article suggest [sic] the use of digital timing in a cardiac pacer * * *."

Dr. Cywinski, an expert in the cardiac pacer art, states in his affidavit:

> In 1967 * * * I met Neil Moore [co-author of Walsh] and learned of a digital timing unit which he and Leon Walsh had built and were using for their stimulation studies. * * * I have been shown a 1966 article [Walsh]. * * * I recognized the apparatus referenced therein as being that which was described to me [by Moore] in 1967 or 1968. At this time (1967-1968), I was also aware of other medical research devices employing digital counters as timing chains.
>
> Even before this period, it was becoming increasingly common to employ digital timing techniques in research environments. The digital approach was indicated where precise incremental timing was needed or where considerable flexibility and repeatable adjustments were needed. These characteristics are typically needed in investigatory or research projects.
>
> * * *
>
> Of the various prior art laboratory timing devices employing digital counting chains, it should also be noted that these were largely operator-controlled devices. * * *
>
> Although I was thus quite familiar with the use of digital timing devices as laboratory instruments, I was nonetheless impressed with the *novelty* of the digital cardiac pacer, being developed by Cordis, which was first described to me by John Walter Keller in about 1970 in a form of a personal communication. This pacer is described and claimed in U.S. Patent No. 3,557,796. *At the time, I did not regard the approach described to me by Keller as being obvious.* Rather, I believed that the approach would not have been obvious even to try since the complexity would seem to outweigh the advantages of digital timing. Further, the usual advantages, i.e., exceptional precision and incremental adjustability, were not ones which would appear to have particular utility in cardiac pacers. Rather, the simplicity of the usual analog timing circuit would seem to offer the clear advantages. I should note that *I was, at that time, also familiar with the Cordis synchronous pacer which is disclosed and claimed in Keller Patent No. 3,253,596 and also the American Optical standby pacer, an earlier version of which is disclosed and claimed in Berkovits Patent No. 3,345,990.*
>
> * * *
>
> The Cordis pacer is a therapeutic device rather than a research tool and, further, is interactive with the spontaneous action of the patient's heart. The device disclosed in the Moore et al. article does not in any similar way respond to naturally occurring heart signals nor am I aware of any other prior art device in which a *digital* counting chain is preset in response to a naturally occurring heartbeat. * * * The heart being stimulated [in Walsh] is an object of study, not an organism being aided in its natural function. * * * I do not find *in* the Walsh et al. article any suggestion that these attributes [higher degree of accuracy and resetability when digital timing circuitry is used instead of analog timing circuitry] would be advantageous in a cardiac pacer.
>
> A cardiac pacer is *implanted* in the human body to monitor and control * * * the heart * * * to continue the life of the patient * * * with no wire connections to the world outside the patient's body.
>
> * * *
>
> [O]ne skilled in the art at the time of the Keller et al. invention would not expect that it would be either desirable or advantageous to use complicated digital circuitry. Nor would one appreciate the great advantage of the digital approach, an approach which in practice has now become recognized by the industry. [Emphasis added.]

No other rebuttal evidence was offered. The examiner did not present any additional evidence in response to the affidavit.

Board Opinion

The board unanimously affirmed the rejection of claims 1, 2, 6, 7, and 13-16 under 35 USC 251, and entered the rejection of claims 9-12 on the same ground.

The board was divided regarding the art rejections. Two members found the affidavit insufficient to overcome the prima facie case of obviousness established by the examiner and affirmed these rejections. The majority

opinion states that the affiant's statements "that he was impressed with the novelty, did not regard the approach as being obvious and believed that the approach would not have been obvious even to try * * * [are] statements [of] affiant's opinion on the ultimate legal issue and, therefore, are entitled to little weight [citations omitted]."

Regarding Dr. Cywinski's factual statements about the prior art, the opinion states:

> The points made by affiant are well-taken but, to a large extent not germane to the claimed subject matter or the rejections under section 103. * * * [The affiant] addressed himself to the intended purpose, and, undoubtedly the actual commercial purpose, of the claimed subject matter. However, the claims are not directed to a therapeutic cardiac pacer which is to be implanted into a human body to monitor and control the heart in order to continue the life of the patient. The claims are broad enough to encompass a device for use on animals in a research laboratory * * *.

The board held:

> Keller and Berkovits both disclose cardiac pacers which function in a manner similar to the appellants' pacer using an analog timer. Walsh discloses a heart stimulator wherein a digital timer is used. The motivation for using a digital timer in place of the analog timer in the Keller and Berkovits pacers is found in Walsh where it is stated, at page 30, that digital timers provide a higher degree of accuracy as compared with analog timers.
> The rejections under section 103 are predicated on replacing the analog R-C timing means in Keller and Berkovits with an equivalent digital timer; not on combining the Walsh device with the Keller or Berkovits pacer or substituting the Walsh device for the R-C timing circuit of Keller or Berkovits. * * * The fact that the Walsh reference makes no mention of pacing a heart or that the Walsh device does not respond to naturally occurring heart signals is immaterial. *The Walsh reference is only relied on for the teaching of digital timing in an analogous environment; the other features are disclosed in Keller and Berkovits.* [Emphasis added.]

The third member of the board found the affidavit sufficient to overcome the prima facie case of obviousness established by the examiner. He stated that the affiant makes "several pertinent statements which must be considered as facts because they are being made by an expert and cannot be dismissed as mere opinion." He also stated that "to say in the claims that the cardiac pacer is to be implanted in a human being to monitor and control the heart for the purpose of sustaining life would be, in my opinion, redundant."

Opinion

Appellant does not argue that any features of the rejected claims other than the use of digital timing are not disclosed in Keller and Berkovits. Thus, the sole issue regarding the prior art rejections is essentially whether the references, taken collectively, would have suggested the use of digital timing in a cardiac pacer to those of ordinary skill in the art at the time the invention was made.[10]

Appellant argues essentially three points:

(1) the teachings of Walsh cannot properly be combined with those of either Keller or Berkovits because Walsh does not relate to a cardiac pacer;
(2) if the digital timing circuitry taught by Walsh is incorporated in either the Keller pacer or the Berkovits pacer, the resulting structure would not fairly meet the claims in issue; and
(3) the board did not "accord appropriate weight to" Dr. Cywinski's affidavit, but rather "completely set aside", "disregarded", and "ignored" his statements therein.

Definition of Cardiac Pacer

[1] The claims are directed to cardiac pacer apparatus. A cardiac pacer is defined as:

> * * * a device designed to stimulate, by electrical impulse, contractions of the heart muscle at a certain rate; used in absence of normal function of the

[10] Miniaturization of the physical size of the circuitry used in a cardiac pacer, the use of integrated circuit techniques in such circuitry, the elimination of hand-wired circuit interconnections in such circuitry, and so forth are not in issue. These features are not claim limitations. Moreover, appellant admits that

> * * * integrated circuits were used in analog pacers and an integrated circuit amplifier was incorporated in the first digitally timed cardiac pacer made by Cordis Corporation * * *. The choice between analog timing and digital timing was thus made largely independently of the move to integrated circuits.

> sino-atrial node; it may be connected from the outside or implanted within the body.[1]

On its face, Keller relates to a cardiac pacer which is implanted within the body. On its face, Berkovits relates to a cardiac pacer which is not implantable within the body, but rather is connected from the outside of the patient's body. Appellant admitted below that "[b]oth the Keller '596 patent and the Berkovits '990 patent disclose cardiac pacers * * *," and asserted that these patents "represent conventional thinking with respect to cardiac pacing at the time the present invention was made." Appellant admitted further that "the Keller et al. and Berkovits devices are true interactive cardiac pacers * * *." Thus, the term "cardiac pacer" encompasses both implantable and non-implantable devices. Therefore, the words "cardiac pacer apparatus" used in the rejected claims are broad enough to read on a device for humans which is not implanted.[12]

Walsh Relates to Analogous Art

Contrary to the position advanced by appellant on appeal, Keller and Berkovits are the principal references relied on by the examiner in his rejections.[13] Walsh is the secondary reference. The board correctly noted that Walsh is relied on only for the teaching of digital timing in an analogous environment.

Appellant "strongly emphasizes" that Walsh "is not about cardiac pacing"; and that the device taught by Walsh is an investigatory device used in the study of a mammalian heart rather than a therapeutic device used in the treatment of a living human (which, of course, has a mammalian heart).

[2] Walsh discloses a heart stimulator used in studies of the atrioventricular conduction system of a mammalian heart. A stimulator used in studies of the atrioventricular conduction system of a mammalian heart is not so non-analogous to a stimulator used to pace a mammalian heart that it should be ignored. Accordingly, Walsh may be combined with either Keller or Berkovits. In re Menough, 51 CCPA 741, 323 F.2d 1011, 139 USPQ 278 (1963).

Appellant further argues that Walsh does not relate to a cardiac pacer because Walsh teaches a stimulator which is used in conjunction with an oscilloscope, and which has a multiplicity of multiple position switches that are operator controlled. As discussed above, Berkovits discloses a cardiac pacer which may be used in conjunction with an oscilloscope, and which has a multiplicity of multiple position switches as well as other variable circuit elements that are operator controlled. Thus, the argument that such features render Walsh unrelated to a cardiac pacer is without merit.

Combining Walsh with Keller or Berkovits

[3, 4] To justify combining reference teachings in support of a rejection it is not necessary that a device shown in one reference can be physically inserted into the device shown in the other. In re Griver, 53 CCPA 815, 354, F.2d 377, 148 USPQ 197 (1966); In re Billingsley, 47 CCPA 1108, 279 F.2d 689, 126 USPQ 370 (1960). The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Wood, 599 F.2d 1032, 202 USPQ 171 (CCPA 1979); In re Passal, 57 CCPA 1151, 426 F.2d 828, 165 USPQ 720 (1970); In re Richman, 57 CCPA 1060, 424 F.2d 1388, 165 USPQ 509 (1970); In re Rosselet, 52 CCPA 1533, 347 F.2d 847, 146 USPQ 183 (1965).

Both Keller and Berkovits disclose heart stimulators that use R-C type timing circuits. Walsh teaches the use of digital type timing circuits in place of R-C type timing circuits in conventional heart stimulators. Therefore, the question is whether it would have been obvious to one of ordinary skill in the art, working with the Keller and the Berkovits and the Walsh references before

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[11] Dorland's Illustrated Medical Dictionary 1080-81 (24th ed. 1965), defining "pacemaker." This definition is carried forward in the subsequent edition, Dorland's Illustrated Medical Dictionary 1117-18 (25th ed. 1974), and augmented with examples of external types and implanted types of pacers.

[12] Dr. Cywinski, who indicated that he was familiar with the pacers "disclosed and claimed" in Keller and in Berkovits, stated: "A cardiac pacer is implanted in the human body to * * *." We note Dr. Cywinski did not state that a device cannot be a cardiac pacer if it is not implanted in the human body, and we further note that, based on his familiarity with the pacer disclosed and claimed in Berkovits (which is not implantable), he could not have intended his testimony to be so construed.

[13] Appellant, at page 6 of his main brief, states: "* * * the type described in the principal reference, the Walsh et al. article."

him, to do what the inventors herein have done, that is, to use a digital timing circuit in a cardiac pacer. In re Winslow, 53 CCPA 1574, 365 F.2d 1017, 151 USPQ 48 (1966), as modified by In re Antle, 58 CCPA 1382, 444 F.2d 1168, 170 USPQ 285 (1971). We agree that the references establish a prima facie case of obviousness.

The Cywinski Affidavit

[5] Once a prima facie case of obviousness was established below, the burden shifted to appellant to rebut it, if he could, with objective evidence of non-obviousness. In re Fielder, 471 F.2d 640, 176 USPQ 300 (CCPA 1973). Appellant attempted to do so by introducing the Cywinski affidavit. Both this court and the PTO must give full consideration to that evidence and render a decision based on the relative strength of appellant's showing and the prima facie case established by the references. In re Saunders, 58 CCPA 1316, 444 F.2d 599, 170 USPQ 213 (1971).

Appellant's showing below "*may* well shift the burden of proof to the examiner to then come forward with further support for his conclusion that the invention would be obvious under the conditions stated in section 103." In re Katzschmann, 52 CCPA 1497, 1500, 347 F.2d 620, 622, 146 USPQ 66, 68 (1965). (Emphasis added.) Whether appellant's showing does shift the burden of proof, however, must be determined on a case by case basis.

[6] As characterized by appellant, the Cywinski affidavit offered as objective evidence of non-obviousness "concerns itself mainly with the question of whether the Walsh et al. article suggest [sic] the use of digital timing in a cardiac pacer * * *." But one cannot show non-obviousness by attacking references individually where, as here, the rejections are based on combinations of references. In re Young, 56 CCPA 757, 403 F.2d 754, 159 USPQ 725 (1968). Moreover, as set forth above, the test is not whether a suggestion to use digital timing in a cardiac pacer is found *in* Walsh (which was the test applied by Dr. Cywinski), but rather what Keller in view of Walsh and what Berkovits in view of Walsh would have suggested to one of ordinary skill in the art.

Contrary to the position advanced by appellant, In re Carroll, 601 F.2d 1184, 202 USPQ 571 (CCPA 1979) is not "nearly 'on fours' with the present factual situation."

In Carroll this court concluded that the opinion of an expert on what the prior art taught was deserving of considerable deference under the circumstances of that case. The expert had critically reviewed the sole piece of prior art and totally discounted its value. The accuracy of the expert's views was supported by documentary evidence.

[7] In the present case, we are not presented with a single prior art reference, but rather two combinations of three references: Keller in view of Walsh, and Berkovits in view of Walsh. The affidavit does not indicate that Dr. Cywinski critically reviewed the use of digital timing in a cardiac pacer as prima facie established by the two combinations of references. Consequently, Dr. Cywinski's opinion on the ultimate legal question of obviousness is entitled to little weight.

Section 103 Rejections are Affirmed

The board considered Dr. Cywinski's testimony and accorded it due weight. We are satisfied that the record herein contains sufficient evidence to support the board's decision. Accordingly, we affirm the decision of the board regarding the §103 rejections.

Requirements of Reissue Declaration

Turning to the rejections under 35 USC 251, we note that a reissue declaration, defective in the nature alleged herein, is correctable in the PTO by the filing of a supplemental oath or declaration.

[8] A reissue oath or declaration filed under 37 CFR 1.175 subsection (a)(4) must also comply with both subsections (a)(5) and (a)(6).[4] Subsection (a) of section 1.175 sets forth requirements relating to the *content* of a statement which must be filed by the applicant with his reissue application. Subsection (a)(4), which requires the applicant to particularly specify the prior art or other information relevant to patentability and not previously considered by the PTO, which might cause the examiner to deem the original patent wholly or partly inoperative or invalid, therefore requires the prior art or other information to be specified *in* that statement.

In the present case, the reissue declaration purported to incorporate by reference a paper entitled "citation to prior art" on which the prior art being brought to the attention of the PTO by the applicant was delineated. The question before this court, therefore, is whether the citation of prior art was successfully incorporated by reference into the declaration.

[4] See note 4, supra.

[9] Subsection (a) of section 1.175 requires the statement to be made by the applicant under oath or declaration. This statement, therefore, (1) must be subscribed to by the applicant, and (2) must either (a) be sworn to or affirmed by the applicant as provided in 37 CFR 1.66, or (b) include the personal declaration of the applicant as prescribed in 37 CFR 1.68. See 37 CFR 1.65(a)(2).

In the present case, the declaration per se was subscribed by the applicant and included an appropriate personal declaration of the applicant. The citation of prior art was not subscribed by the applicant and did not include the personal declaration of the applicant. Rather, the citation of prior art was subscribed by applicant's attorney. And, while the citation of prior art is dated one day earlier than the declaration, there is no evidence in the record that applicant even saw the citation of prior art at the time the declaration was executed.

[10] Accordingly, we affirm the decision of the board regarding the rejections of claims 1, 2, 6, 7, and 9-16 under 35 USC 251 because the declaration does not comply with 37 CFR 1.175(a)(4).

As to the rejections on grounds relating to 37 CFR 1.175(a)(5) and (a)(6), we do not agree with the board.

Subsection (a)(5) requires the applicant to specify "the errors or what might be deemed to be errors relied upon, and how they arose or occurred." Subsection 1414.03 of the Manual of Patent Examining Procedure (MPEP) (4th ed., Rev. 1, Jan. 1980)[15] states that to comply with the requirements of subsection (a)(5) in a §1.175(a)(4) type reissue, the reissue declaration.

> might state that some or all claims might be deemed to be too broad and invalid in view of references X and Y which were not of record in the patent files. Usually, a general statement will suffice. * * * [The reissue declaration] must indicate when and the manner in which the reissue applicant became aware of the prior art or other information. * * *

MPEP §1401.08 (3rd ed., Rev. 54, Oct. 1977) merely stated:

> The reissue oath or declaration must point out very specifically what the defects are and how the errors arose.

Applicant's reissue declaration contains a passage (which we have numbered "1" in the quoted declaration) that is remarkably close to what subsequently appeared in the fourth edition of the MPEP with respect to the content of a declaration for this purpose. We hold on the facts of this case that the declaration fairly meets the requirements of 37 CFR 1.175(a)(5).

Subsection (a)(6) requires the applicant to state that said errors, if any, arose without deceptive intention on the part of the applicant. The passage in the declaration which we have numbered "3" fairly meets this requirement.

Conclusion

Accordingly, the decision of the board regarding the rejections of claims 1, 2, 6, 7, 9-11, 13, and 14 based on the prior art is *affirmed*, the decision of the board regarding the rejections of claims 1, 2, 6, 7, and 9-16 based on 37 CFR 1.175 subsection (a)(4) is *affirmed*, and that based on subsections (a)(5) and (a)(6) is *reversed*.

Modified.

U.S. Court of Claims

Lemelson v. United States et al.

Nos. 414-79C and 415-79C
Decided Nov. 28, 1980

PATENTS

1. Court of Claims — Pleading and practice (§27.7)

Pleading and practice in courts — Discovery and inspection (§53.30)

Discovery of nongovernmental sales information from third-party defendants while validity of patent is still in dispute is not necessarily premature; Kaufman v. United States, 173 USPQ 806, rejected implicitly underlying rationale of Burndy v. Sealectro, 137 USPQ 303, that trial court cannot allow discovery of commercial sales to help establish patent's validity.

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[15] We note that MPEP chapter 1400, the chapter dealing with reissue applications, has been completely revised in the fourth edition and now includes detailed instructions regarding, inter alia, reissue declarations.

disposition would render moot Goehring's appeal from the denial of summary judgment on the antitrust issue. I would also vacate the district court's summary judgment on patent misuse which arose from the improvident grant of the motion to amend. I would accordingly direct that the proceedings be taken up again from the state they were in prior to the granting of the motion for leave to amend on December 5, 1984. I do not reach the res judicata issue nor issues certified to us, as my disposition would render them moot in this case.

Court of Appeals, Federal Circuit

In re Merck & Co., Inc.

No. 85-2740

Decided September 8, 1986

PATENTS

1. Patentability — Invention — Specific cases — Chemical (§51.5093)

Board of Patent Appeals and Interferences' decision sustaining rejection for obviousness of reexamination claims for antidepressant drug amitriptyline was proper, since claimed drug is structurally similar to other prior art psychotropic compound, imipramine, which is known to possess antidepressive properties, and thus one skilled in medicinal chemical arts would have expected amitriptyline to resemble imipramine in alleviation of depression in humans.

Appeal from Patent and Trademark Office Board of Patent Appeals and Interferences.

Reexamination request, Control No. 90/000264, to reexamine patent of Edward L. Englehardt, Patent No. 3,428,735, issued February 18, 1969, on application, Serial No. 662,907, filed August 24, 1967, as continuation-in-part of application Serial No. 855,981, filed November 30, 1959. From decision sustaining decision rejecting claims 1-3 in reexamination application, applicant appeals. Affirmed; Baldwin, Circuit Judge, dissenting with opinion.

Charles M. Caruso, Rahway, N.J. (Nels T. Lippert, and Fitzpatrick, Cella, Harper & Scinto, New York, N.Y., on the brief, and Mario A. Monaco, and Michael C. Sudol, Jr., both of Rahway, N.J., of counsel) for appellant.

Richard E. Schafer, Associate Solicitor (Joseph F. Nakamura, Solicitor, and Fred E. McKelvey, Deputy Solicitor, on the brief) for Patent and Trademark Office.

Donald R. Dunner, and Finnegan, Henderson, Farabow, Garrett & Dunner, both of Washington, D.C. (Robert D. Bajefsky, Carol P. Einaudi, and Finnegan, Henderson, Farabow, Garrett & Dunner, all of Washington, D.C., on the brief, and Beryl L. Snyder, Elmwood Park, N.J., of counsel) for intervenor Biocraft Laboratories, Inc.

Before Davis, Baldwin, and Archer, Circuit Judges.

Davis, Circuit Judge.

This is an appeal from a final decision of the United States Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences (Board), sustaining the rejection of claims 1 through 3 in the reexamination application[1] of U.S. Patent No. 3,428,735[2] (the '735 patent) as unpatentable under 35 U.S.C. § 103. We affirm.

I. BACKGROUND

A. *The Invention*

The invention is directed to a method of treating human mental disorders; the method involves treating depression in humans by the oral administration of 5-(3-dimethylaminopropylidene) dibenzo[a,d] [1,4] cycloheptadiene (commonly known as and hereafter referred to as "amitriptyline"), or the hydrochloride or hydrobromide salts thereof,

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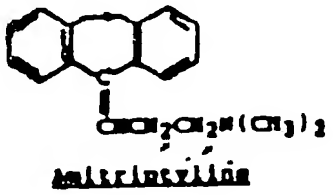
[1] *Ex Parte Merck and Co.*, Reexamination No. 90/000264, Appeal No. 607-66 (PTO Bd. Pat. App. & Int., May 28, 1985), JA p.7. In its opinion the Board expressly adopted the reasonings in its earlier reissue (for the '735 patent) opinions, *Ex Parte Edward L. Engelhardt*, Reissue Application No. 776,464, Appeal No. 424-40 (PTO Bd. Pat. App., Apr. 23, 1980), JA p. 13 and *Ex Parte Edward L. Engelhardt*, Reissue Application No. 776, 464, Appeal No. 480-01 (PTO Bd. Pat. App., Fed. 25, 1982), JA p. 23.

[2] U.S. Patent No. 3,428,735, issued to Edward L. Engelhardt on February 18, 1969, was based on patent application Serial No. 662,907 filed August 24, 1967 as a continuation-in-part of patent application Serial No. 855,981 filed Nov. 30, 1959.

in a particular dosage range. Amitriptyline has the following chemical structure:



As representative of the invention, claim 1 reads:

> 1. A method of treating human mental disorders involving depression which comprises orally administering to a human affected by depression 5-(3-dimethylamino-propylidene) dibenzo [a,d] [1,4] cycloheptadiene or its non-toxic salts in daily dosage of 25 to 250 mg. of said compound.

Remaining claims 2 and 3 are dependent from claim 1 and add limitations pertaining to the use of the hydrochloride and hydrobromide salts of amitriptyline, respectively.

B. *Related Proceedings*

On March 10, 1977 an application, Serial No. 776,464 (the '464 application), was filed for reissue of the '735 patent.[3] All the claims of the '464 application were finally rejected by the examiner under section 102 of title 35, United States Code, and alternatively under section 103 of that title. Subsequently, an appeal (Appeal No. 424–40) was taken to the Board[4] which affirmed the examiner's rejections. Additionally, the Board entered a new rejection under 35 U.S.C. § 103 over a combination of references not previously cited by the examiner. In accordance with 37 C.F.R. § 1.196(b) (1985)[5], appellant elected reconsideration of the '464 application by the examiner. The examiner maintained the rejection entered by the Board; in Appeal No. 480–01, the Board affirmed the examiner. The Board's decision was appealed to the Court of Customs and Patent Appeals (CCPA). Upon the motion of the Commissioner of Patents and Trademarks and on the authority of *In re Dien*, 680 F.2d 151, 214 USPQ 10 (CCPA 1982), the appeal was dismissed for lack of subject matter jurisdiction.[6]

The reissue application was protested by Biocraft Laboratories, Inc. (Biocraft), intervenor in the current appeal. Biocraft is also the plaintiff in a related litigation pending in the U.S. District Court for the District of New Jersey in which the validity and infringement of the '735 patent is in issue. *See Biocraft Laboratories Inc. v. Merck & Co.*, Civil Action No. 77–0693 (D.N.J.). The district court has stayed further action in that case pending the final outcome of the pending PTO proceedings.

C. *Reexamination Proceeding*

Following dismissal of the reissue appeal by the CCPA, Merck & Co., Inc. (Merck), the assignee of the '735 patent, filed for and was granted a request for reexamination of the patent. As a result of prosecution before the examiner, claims 1 through 3 of the reexamination application were finally rejected under 35 U.S.C. § 102 as anticipated by prior art references; the claims were also rejected under 35 U.S.C. § 103 as being obvious over references cited by the Board in its new ground of rejection entered during the initial reissue appeal. Finding the '735 patent to be entitled to the benefit of the November 30, 1959 filing date of its parent application, Serial No. 855,981, the Board reversed the section 102 rejection because the effective filing date of the application antedated all the references cited therein. The Board, however, sustained the rejection for obviousness under section 103. Expressly adopting the reasonings of its earlier reissue opinions, the Board took the position that in view of the prior art, in combination, and a thorough knowledge of the investigative techniques used in the medicinal chemical art, the skilled artisan would have expected the known tricyclic compound, amitriptyline, to be useful as an antidepressant.

D. *The References*

The references relied upon by the Board were:

(1) Rey-Bellet et all (Rey-Bellet) U.S. Patent No. 3,384,663, May 21, 1968 (application filed Mar. 27, 1959);

(2) Kuhn, *Schweizerische Medizinische Wochenschrift*, Vol. 87, No. 35–36, pp. 1135–1140 (Aug. 1957)

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[3] The reissue application was filed as a "no defect" type reissue under the then existing 37 C.F.R. § 1.175(a)(4) (1980). That provision has now been repealed..

[4] At that time, the Board of Patent Appeals and Interferences was called the Board of Patent Appeals.

[5] 37 C.F.R. § 1.196(b) provides that when the Board of Appeals determines a new ground of rejection, the appellant may

(1) after submitting appropriate amendments or showing of facts, have the matter reconsidered by the examiner;

(2) waive reconsideration before the examiner and have the case reconsidered by the Board; or

(3) treat the decision, including the new ground of rejection, as a final decision in the case.

[6] *See In the Matter of the Application of Edward L. Engelhardt*, Appeal No. 82–611 (CAFC Oct. 28, 1982) (order granting motion to dismiss).

(3) Lehman et al. (Lehman), *Canadian Psychiatric Association Journal*, "The Treatment of Depressive Conditions with Imipramine (G 22355)", vol. 3, No. 4, pp. 155–164 (Oct. 1958);

(4) Friedman, *First Symposium On Chemical Biological Correlation*, "Influence of Isosteric Replacements Upon Biological Activity", pp. 296–358 (May 1950);

(5) Burger, *Journal of Chemical Education*, "Rational Approaches to Drug Structure", Vol. 33, No. 8, pp. 362–372 (Aug. 1956);

(6) Petersen et al. (Petersen), *Arzneimittel-Forschung*, Vol. 8, No. 7, pp. 395–397 (1958);

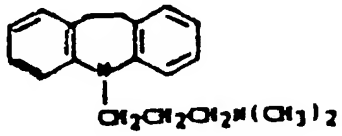
(7) Roche Research Report No. 43,162, pp. 1–9 (Nov. 1957);

(8) Roche Research Report No. 43,169, pp. 1–8 (Apr. 1958);

(9) Roche Research Report No. 52,195, pp. 1–13 (Sept. 1958) (Collectively called the "Roche Reports").

The Rey-Bellet patent disclosed amitriptyline and its hydrochloride salt. Properties of amitriptyline taught by the reference included a "manifold activity upon the central nervous system," as well as pharmacological and medicinal properties, such as "narcosis-potentiating, adrenolytic, sedative, antihistaminic, antiemetic, antipyretic and hypothermic." Rey-Bellet did not disclose or otherwise teach that amitriptyline possessed antidepressive properties.

The Kuhn publication disclosed the compound, imipramine, and taught that the compound was a very effective antidepressant in humans. Imipramine has the chemical structure



Imipramine

and differs from the structure of amitriptyline only in the replacement of the unsaturated carbon atom in the center ring with a nitrogen atom. Kuhn taught a recommended dosage of 75–150 mg per day — possibly 200–250 mg if the smaller doses proved ineffective.

The Lehman publication disclosed the results of a Canadian study of the effects of imipramine on the symptons of depression in humans. This article confirmed, for the most part, the teachings of the Kuhn article.

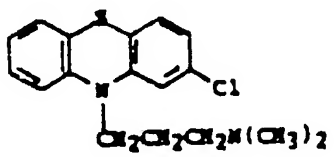
The object of the Freidman publication was "to survey the history of isosterism, to classify the varieties of isosteric replacements which are recorded in the literature, and to note the influence of these replacements on the biological activity of compounds." Friedman defined isosteres as atoms, ions or molecules in which the peripheral layers of electrons can be considered identical. Compounds which fit this broad definition and exhibit the same biological activity were termed "bioisosteric." Further, with respect to the medicinal chemists' use of the theory of "isosteric replacement" or "bio-isosteric replacement" as a tool to predict the properties of compounds, Friedman commented that:

> [t]o the synthetic organic chemist interested in medicinal chemistry, every physiologically active compound of known structure is a challenge – a challenge either to better it, or perhaps merely to equal it. . . .
>
> There are numerous ways of attacking such a problem. . . . One of the methods which has been used frequently, very often with success, is that of isosteric replacement. The examples of this type of replacement in the literature are very numerous, and the fruitful results in the fields of sulfonamides, antimetabolites, and antihistamines are well known.

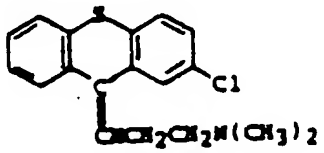
Friedman at page 296. Finally, Friedman disclosed various atoms or groups of atoms as bioisosteric, including the interchange of oxygen and the unsaturated carbon atom which often resulted in similar biological activity. Friedman, however, did not disclose or otherwise teach as bioisoteric the interchange of the nitrogen and unsaturated carbon atoms.

The Burger publication also discussed the theory of "bioisosterism" and its usefulness in designing new drugs based upon the knowledge of "lead" compounds.

The Petersen publication taught, *inter alia*, the properties of chlorpromazine (a phenothiazine derivative) and chlorprothixene (a 9-amino-alkylene-thioxanthene derivative), these compounds have the following structural formulas:



Chlorpromazine



Chlorprothixene

Petersen concluded that, when the nitrogen atom located in the central ring of the phenothiazine compound is interchanged with an unsaturated carbon atom as in the corresponding 9-amino-alkylene-thioxanthene compound, the pharmocological properties of the thioxanthene derivatives resemble very strongly the properties of the corresponding phenothiazines. Using the theory of isosteric replacement, Petersen predicted this similarity in properties:

> Structural chemical considerations permitted the expectation that the 9-aminoalkylene-thioxanthenes ... would show great similarity to the corresponding phenothiazines. They should be more similar in their behavior to that of the phenothiazines than the saturated 9-aminoalkyl-thioxanthenes. From the physical point of view the π-electron distributions (sites of π - electrons) are almost the same in the phenothiazine derivatives and in the 9-aminoalkylene-thioxanthenes with their stabilizing conjugated double linkage between C9 in the thioxanthene ring and the first C-atom of the side chain.

Petersen at page 3. The compounds were disclosed as having a strong central depressive, i.e., tranquillizing, action in animals.

The Roche Reports revealed the results from tests comparing the pharmacological properties of amitriptyline and imipramine. The reports indicated that the two compounds were very similar in a variety of properties, including their action as tranquilizers having narcosis-potentiating effects. Because of this similarity and because amitriptyline and imipramine were structurally related, Roche scientists concluded that amitriptyline should be clinically tested for depression alleviation — a known property of imipramine. In the pharmalogical guideline for the clinical testings of amitriptyline (which was labelled Roche Preparation Ro 4-1575), the Roche Reports stated that

> [i]t is to be noted that a "tofranil-like effect" is already to be expected by using a dose ¼ — ½ that of Tofranil. Side effects which can appear ... are sedative and atropine-like effects, such as appear also with Tofranil.[1]

We must decide in this appeal whether appellant's invention would have been prima facie obvious over the available prior art of record; and, if so obvious, whether the prima facie case has been rebutted by evidence of unexpected results.

III. DISCUSSION

In its opinion on this problem, the Board expressly followed the guidelines of *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 466-67 (1966), and made findings on factual inquiries specifically set forth in that decision. These factual findings must be accepted unless they are clearly erroneous. *In re Wilder*, 736 F.2d 1516, 1520, 222 USPQ 369, 372 (Fed. Cir. 1984), *cert. denied*, 105 S.Ct. 1173 (1985); *In re De Blauwe*, 736 F.2d 699, 703, 222 USPQ 191, 193 (Fed. Cir. 1984); *accord Stock Pot Restaurant, Inc. v. Stockpot, Inc.*, 737 F.2d 1576, 1578-79, 222 USPQ 665, 666-67 (Fed. Cir. 1984). In this case we do not hold the Board's factual findings — as to the scope and content of the prior art, the differences between the prior art and the claims at issue, and the level of ordinary skill in the art — to be clearly erroneous and accordingly we have followed them in our statement of the prior art and we now follow them in our analysis of the legal issue of obviousness.

Prima Facie Obviousness: The prior art taught that amitriptyline and imipramine are both psychotropic drugs which react on the central nervous system and which were known in the art prior to the time of appellant's invention. Imipramine was known to possess antidepressive properties in humans. While amitriptyline was known to possess psychotropic properties such as sedative and narcosis-potentiating properties, the drug was not known to be an antidepressant. However, the prior art has shown that imipramine and amitriptyline are unquestionably closely related in structure. Both compounds are tricyclic dibenzo compounds and differ structurally only in that the nitrogen atom located in the central ring of imipramine is interchanged with an unsaturated carbon atom in the central ring of amitriptyline. To show obviousness, it was necessary to determine from knowledge already available in the art at the time of appellant's invention that one skilled in the medicinal chemical art would have expected amitriptyline, like imipramine, to be useful in the treatment of depression in humans. *In re*

[1] Tofranil is a tradename used for imipramine.

Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

As found by the Board, the Roche Reports recognized the structural relationship between amitriptyline and imipramine and concluded that amitriptyline should be tested for its antidepressant activities. In fact the Roche Reports expressly stated that amitriptyline was expected to resemble imipramine clinically in its depression alleviation effects.

"Structural similarity, alone, may be sufficient to give rise to an expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). However, the Board did not rest its conclusion of obviousness on structural similarity alone. Rather, the Board further recognized that in attempting to predict the biological activities of a drug, a skilled medicinal chemist would not proceed randomly, but would base his attempts on the available knowledge of prior research techniques, and literature used in his field. The prior art showed that one such technique was "bioisosteric replacement" or the theory of bioisosterism — where the substitution of one atom or group of atoms for another atom or group of atoms having similar size, shape and electron density provides molecules having the same type of biological activity. Finding that the Friedman, Burger and Petersen references taught that bioisosterism was commonly used by medicinal chemists prior to 1959 in an effort to design and predict drug activity, the Board concluded that one of ordinary skill in the arts would have been aware of this technique at the time of appellant's invention.[8] Further, the Board found that Petersen taught as bioisosteric the interchange of the nitrogen and unsaturated carbon atoms — the precise structural difference between imipramine and amitriptyline.[9]

We see no clear error in the Board's determination as to the teachings of the prior art references, in combination. In view of these teachings, which show a close structural similarity and a similar use (psychotropic drugs) between amitriptyline and imipramine, one of ordinary skill in the medicinal chemical arts, possessed of the knowledge of the investigative techniques used in the field of drug design and pharmacological predictability, would have expected amitriptyline to resemble imipramine in the alleviation of depression in humans. Accordingly, we agree with the Board that appellant's invention was prima facie obvious over the prior art of record.

In traversing the Board's decision of obviousness, appellant has urged that the Board's decision was premised on an impermissible "obvious to try" standard. Appellant contends that there was no motivation in the prior art to arrive at appellant's invention. "[O]bvious to try is not the standard of 35 U.S.C. § 103." *In re Antonie*, 559 F.2d 618, 620, 195 USPQ 6, 8 (CCPA 1977) (emphasis omitted). Rather, the test is whether the references, taken as a whole, would have suggested appellant's invention to one of ordinary skill in the medicinal chemical arts at the time the invention was made. *In re Simon*, 461 F.2d 1387, 1390, 174 USPQ 114, 116 (CCPA 1972). Clearly, amitriptyline and imipramine, both known psychotropic drugs, are closely structurally related. The expectation that the similar structures would behave similarly was suggested in the Roche Reports. In combination with those teachings, the prior art teaching that the precise structural difference between amitriptyline and imipramine involves a known bioisosteric replacement provides sufficient basis for the required expectation of success, without resort to hindsight.[10] Obviousness does not require absolute predictability. *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976). Only a reasonable expectation that the beneficial result will be achieved is necessary to show obviousness. *In re Longi*,

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[8] Appellant submitted the declaration of Dr. Paul N. Craig, an experienced medicinal chemist, JA p. 372. His view was that the concept of bioisosterism could not be used in 1959 to predict the antidepressant effects in amitriptyline or the pharmacological differences between imipramine and amitriptyline. Dr. Craig stated:

> [I]n my opinion "isosterism" in 1959 afforded no basis for predicting the specific pharmaceutical utility in humans, and it is my belief that that is still true today .... I do not believe the carryover of tranquilizing activity from chlorpromazine to chlorprothixene afforded a reasonable basis for predicting the carryover of antidepressant properties from imipramine to amitriptyline.

Affidavit of Paul N. Craig, JA, pp. 374–75.

Plainly the Board was not clearly erroneous in discounting that testimony. There was independent evidence in the record to the contrary. The Friedman, Burger and Petersen references recognize that concept as a means of predicting biological properties in isosterically-related compounds prior to 1959.

[9] Petersen even went so far as to suggest that the apparent bioisosteric relationship between the interchange of the nitrogen and unsaturated carbon atoms led to the design of chloroprothixene in the expectation that the compound would share the same biological activity as chlorpromazine. *See* Petersen, *supra*, at p. 395.

[10] The teachings of the Roche Reports as well as the Petersen reference distinguish this case from *In re Grabiak*, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("there is no motive in the cited art to make the modification required to arrive at appellants' compounds").

759 F.2d 887, 897, 225 USPQ 645, 651 (Fed. Cir. 1985).

We also find untenable appellant's arguments that Petersen teaches away from appellant's invention. Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). Thus, Petersen must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole. That teaching is that the interchange of the nitrogen and the unsaturated carbon atoms is isosteric and compounds so modified are expected to possess similar biological properties.

Neither are we persuaded by appellant's contention that the Board erred in relying on the contemporaneous independent invention of others to support its holding of obviousness.[11] As we have said earlier, the teachings of the prior art references in combination adequately support the Board's conclusion. However, the additional, although unnecessary, evidence of contemporaneous invention is probative of "the level of knowledge in the art at the time the invention was made." *In re Farrenkopf*, 713 F.2d 714, 720, 219 USPQ 1, 6 (Fed. Cir. 1983).

Unexpected Results: A prima facie case of obviousness can be rebutted by evidence of unexpected results. *In re Davis*, 475 F.2d 667, 670, 177 USPQ 381, 384 (CCPA 1973). In rebuttal of the PTO's prima facie case appellant has asserted that, as compared to imipramine, amitriptyline unexpectedly has a more potent sedative and a stronger anticholinergic effect. In support of this contention, appellant has relied on an affidavit of Dr. Joseph J. Schildkraut,[12] a psychiatrist and a Professor of Psychiatry at Harvard, and also on a published record of a symposium of physicians and psychiatrists concerned with the treatment of the depressed patient.[13]

Dr. Schildkraut's affidavit recognizes some pharmacological differences between amitriptyline and imipramine including the fact that amitriptylne is a more potent sedative and has a strong anticholinergic effect than imipramine. Further, Dr. Schildkraut notes that depressed patients have responded differently to amitriptyline and imipramine, some responding to one and not the other or more favorably to one than to the other. For the most part, the record of the cited symposium confirms the differences noted in the Schildkraut affidavit.[14] That record also counseled practicing physicians on choosing from the spectrum of tricyclic antidepressants (a term which includes amitriptyline and imipramine) the particular drug useful for an individual patient.

After a careful consideration of all the evidence, we are persuaded that the Board did not err in determining that the alleged unexpected properties of amitriptyline are not so unexpectedly different from the properties of imipramine, the closest prior art, as to overcome the prima facie showing of obviousness. The prior art of record clearly taught that amitriptyline was a known sedative.[15] The evidence before us (which was, of course, before the Board) further revealed that all tricyclic antidepressant drugs, in general, possess the secondary properties of sedative and anticholinergic effects. Specifically, the record showed that during the prosecution of the reissue application, appellant submitted an article entitled "Using the tricyclic antidepressants" which included a table comparing the properties of known tricyclic antidepressant drugs.[16] Included in these properties were sedative and anticholinergic effects of the known antidepressants.[17] Thus, it appears that the alleged difference in properties between amitriptyline and imipramine is a matter of degree rather than kind. Moreover, as to the sedative effects, the article revealed only a slight difference between the two compounds. Amitriptyline was characterized as "highly sedative" while imipramine was only "somewhat less [sedative] than amitriptyline." [18] Regarding

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[11] *Ex Parte Edward L. Engelhardt*, Appeal No. 424-40, *supra* note 1, at pp. 23-24, JA pp. 22(l)-22(m), where the Board indicated that evidence before it revealed that four other groups of inventors independently and contemporaneously discovered amitriptyline's antidepressant properties using reasoning based on a thorough knowledge of investigative techniques, which included the concept of isosterism, used in the medicinal art area.

[12] Affidavit of Joseph J. Schildkraut, JA p. 366.

[13] Symposium, *Depression Today — Experts Answer Your Questions*, JA p. 309.

[14] Dr. Schildkraut was a member of the symposium.

[15] Rey-Bellet, *supra*, col. 2, line 16.

[16] *Patient Care*, "Using the Tricyclic Antidepressants," pp. 28-33, 39-40, 43-45, 49-52, 57-58, 63-64, 67-68, 71, 75-76, 78, 81 84-85, (May 15, 1979); *see also* Commission's Appendix, pp. CA 17-45.

[17] *See also* the Symposium, *Depression Today — Experts Answer Your Questions*, *supra*, note 13, at p. 315, where Dr. Hollister indicates that when choosing from the spectrum of tricyclic antidepressant drugs, the choice is based on three pharmocological actions including (1) the amount of sedation (2) the amount of anticholinergic effect and (3) the nature of the drugs in primarily blocking the uptake of serotin or norepinephrine.

[18] *Patient Care*, "Using The Tricyclic Antidepressants," *supra* note 16, at p. 50.

the anticholinergic effect, the article showed that both drugs have anticholinergic effects but to a different degree. These are not truly unexpected results. The Board found in one of its reissue opinions (incorporated in the reexamination decision now on appeal): "[i]n regard to the sedative and anticholinergic properties of amitriptyline, we are not convinced that the side effects of this material [amitriptyline] are significantly or unexpectedly different from the level of those properties exerted by the closest prior art antidepressant, imipramine.[19]

The core of it is that, while there are some differences in degree between the properties of amitriptyline and imipramine, the compounds expectedly have the same type of biological activity. In the absence of evidence to show that the properties of the compounds differed in such an appreciable degree that the difference was really unexpected, we do not think that the Board erred in its determination that appellant's evidence was insufficient to rebut the prima facie case. The fact that amitriptyline and imipramine, respectively, helped some patients and not others does not appear significant. As noted by the Board, a difference in structure, although slight, would have been expected to produce some difference in activity.

[1] In sum, we hold that the claimed invention would have been obvious to one of ordinary skill in the art. Accordingly, the decision of the Board is

AFFIRMED.

Baldwin, Circuit Judge, dissenting.

The rejection by the board is flawed because it did not analyze the invention according to the requirement of 35 U.S.C. § 103. The board wrote:

> The issue before us in considering the instant claims on their merits for patentability is whether the artisan having the requisite skill in the pertinent art area and a knowledge of the available prior art would have been motivated to employ amitriptyline in the treatment of human depression.

That is, whether it would have been obvious to try amitriptyline as an antidepressant. Guided by the disclosure of the applicant, the board pieced together information from various patents, journal articles, and papers, and concluded:

> It remains our position that one having ordinary skill in this art are [sic] would have been familiar with the concept of bioisosterism and because of this knowledge would have concluded that the known compound, i.e., amitriptyline, would be *potentially* useful as an antidepressant. [Emphasis ours.]

That is, it would have been obvious to try amitriptyline as an antidepressant. Obvious-to-try is not the test for patentability under 35 U.S.C. § 103. This court and its predecessor, the CCPA, have repeatedly rejected that approach. *In re Godwin*, 576 F.2d 375, 377, 198 USPQ 1, 3 (CCPA 1978); *In re Antoine*, 559 F.2d 618, 620, 195 USPQ 6, 8 (CCPA 1977); *In re Lindell*, 385 F.2d 453, 455, 155 USPQ 521, 523 (CCPA 1967); *In re Tomlinson*, 363 F.2d 928, 150 USPQ 623 (CCPA 1966); *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963); *see also In re Grabiak*, 769 F.2d 729, 226 USPQ 870 (Fed. Cir. 1985).

Congress has also rejected that approach by enacting the second sentence of 35 U.S.C. §103, which states "[p]atentability shall not be negatived by the manner in which the invention was made." The reviser's note on this sentence states "it is immaterial whether it resulted from long toil and experimentation or from a flash of genius."

The obvious-to-try analysis is an attack on the method of making an invention that specifically penalizes people in areas of endeavor where advances are won only by great effort and expense. The pharmaceutical field is particularly hard hit because there is an over abundance of structures that are obvious to try. Consider, for example, the Peterson reference which the majority cites to demonstrate the possibility that a nitrogen atom may be replaced by a double-bonded carbon atom. This journal article records an attempt to find drugs useful for the treatment of endogenous psychoses, i.e., tranquilizers. The researchers tested eighteen chemicals with closely related structures. These materials were injected into mice, and compared for their ability to make the mice fall asleep. The results of these may be tantalizing and useful, but only as a guide for further research. I agree that, based on this information and the other references cited by the board, the researcher with ordinary skill in the art would be motivated to investigate the possibility of substituting a double-bonded carbon atom for nitrogen. The researcher would also be motivated to test every other structural variation in Peterson, as well as a host of others. Under an obvious-to-try analysis, any of these structures which ultimately is shown to be effective as an antidepressant in human beings would be unpatentable because the researcher dared to follow a logical plan.

[19] *Ex Parte Edward L. Engelhardt*, Appeal No. 480–01, supra note 1, at p.12 JA p. 34

The board and the majority also err by reading too much certainty into the teachings of the references. They have not considered the references as a whole. Friedman discusses the phenomenon that compounds with similar chemical structures sometimes behave in a similar fashion in a biological system. Once such a compound has been tested and found to have the same biological activity, it is called "bio-isosteric."[1]

Friedman also teaches that an isosteric compound "may have the same activity as the original, *or more usually* it may have an *antagonistic* effect." (Emphasis added.) Friedman explains that in order to predict biological activity with accuracy, one ideally should know (1) the mechanism by which the original drug acts and (2) what part of the structure of the original drug is critical to the original drug activity.[2] That reference also unequivocally states that comparisons should be made in living systems, but such information is not easily available. That reference relies on *in vitro* testing, and it specifically states that *in vitro* results may or may not correlate with clinical studies. It also clearly states that, for the purposes of its discussion, biological activities such as absorption, distribution, conjugation (detoxification), taste, odor and *side effects of drugs* will be ignored. Friedman concludes that compounds with similar structures need not be bio-isosteric.

The Burger reference does discuss bio-isosterism and its usefulness in designing new drugs. Its evaluation of bio-isosterism as a tool for predicting drug activity is as follows:

> However, if one can achieve a gradual change of biological behavior and follow it accurately at each step of minor structural alteration, one is bound to enhance one property, suppress another, and ultimately arrive at a drug suitable for therapy. Shortcuts to this disconcertingly tedious process have not been found, and this is probably responsible for the still prevailing opinion that new useful drugs will be discovered most easily by more or less empirical procedures.

at page 369, and

> Slight sterochemical or structural changes may alter considerably the biological role of a compound. Patient variation of at least a reasonable number of structures is still the only answer to this question.

at page 370.

The Roche reports contain background information about various pharmacological effects of amitriptyline. The information was derived from testing for its toxicity and tranquilizing effect on animals. This information would be essential to a decision to clinically test the drug. It is not sufficient to show the drug would be useful for treating human beings. Congress gave pragmatic recognition to the difficulty of determining whether a new drug is useful by its enactment of the 1962 amendment to 21 U.S.C. § 321. That action was taken in response to problems caused by another tranquilizer, thalidomide.

Neither these references, nor the other references cited by the board and the majority purport to teach the worker with ordinary skill in the art that amitriptyline is a drug that is useful for treating depression in human beings. That conclusion is steps removed from the information presented by these sources. I would reverse.

[1] The term "bio-isosteric" therefore is simply a conclusion drawn after testing. The label is properly limited to the system and purpose for which the compounds were tested. For example, two drugs could be bio-isosteric with respect to making mice fall asleep, and not bio-isosteric when tested at a particular dosage level for the treatment of high blood pressure in human beings. The theory of bio-isosterism as used by the board and majority is nothing more or less than an analysis of structural obviousness.

[2] Neither this reference nor any of the others purport to disclose either piece of information.

Court of Appeals, Federal Circuit

George v. Honda Motor Co., Ltd., et al.

No. 85-2612

Decided September 30, 1986

PATENTS

1. Infringement — Substitution of equivalents — In general (§39.751)

Federal district court did not err in granting summary judgment that accused engines do not infringe either literally or under doctrine of equivalents, based upon finding that claimed air-cooled cylinder head structure, unlike accused cylinder which is cooled at least in part by water, does not encompass water-jacket head structure either literally or under doctrine of equivalents.

Particular patents — Engine Cylinders

4,108,118, George, Water Jacket Cylinder, holding of non-infringement affirmed.